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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,833	02/12/2002	Dominique Bourel	065691-0260	8788

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EXAMINER	
SAUNDERS, DAVID A	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 04/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
980,533	BOUREL et al
Examiner	**Group Art Unit**
SAUNDERS	1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☑ Responsive to communication(s) filed on 12/7/01.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☑ Claim(s) 1-29 is/are pending in the application.

Of the above claim(s) 10-24, 26-29 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 1-9, 25 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☑ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☑ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☑ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Action Summary

Amendment of 12/7/01 has been entered. Claims 1-29 are pending and under examination.

Applicant's election without traverse of Group I (claims 1-9 and 25) in Paper No. filed 11/17/03 is acknowledged.

Applicants' election of species of antibodies directed to DNP his been noted.

Claims 1-9 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1 "elevated" is unclear as to what basis is used for determining if the claimed product has an "elevated" reactivity. Is this on a per weight or a per volume basis?

In claim 1 "the activity of the initial polyvalent Igs" lacks antecedent basis for both "activity" and for "the initial polyvalent Igs." Note these recitations also appear in dependent claims 3-4 and 7.

Further, "the activity" is unclear because one dose not know what kind of activity is intended -- activity to treat autoimmune disease, activity to react with one or more of the recited IgMs, IgG F(ab')2s, and DNP?

Also "the initial polyvalent Igs" is unclear as to what makes these "initial". If applicant intends this to refer to some kind of starting preparation of polyvalent Igs, which is subjected to a purification process, then the claim is unclear because no process steps are recited, and one has no idea what may be the nature of "the initial polyvalent Igs" against which the claimed "Ig fraction" must be compared.

Claim 25 depends from non-elected claim 10. Assuming that claim 25 will be independently recited, with the limitations of claim 10 included, the examiner notes the following indefinite aspects of claim 10:

In step a), last line "given autoantigens" is unclear. What makes an autoantigen "given" or not "given"?

Claim 10 (in step e) contains the trademark/trade name TEGELINE. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a preparation of polyvalent IgGs and, accordingly, the identification/description is indefinite.

In the following prior art rejections, species of antibodies against antigens other than DNP will be examined, to the extent that prior art submitted by applicant or found by the examiner may be relevant.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Dietrich et al (Eur Jour Immunol, 22, 1701, 1992).

Dietrich et al disclose the fractionation of IVIg from pooled normal donors via affinity chromatography. The chromatographic support has bound F(ab') 2 fragments that were prepared from IVIg by pepsin digestion. See page 1702, col. 1. The "connected" fraction of antibodies is obtained by absorbing the IVIg preparation on the support washing, and then eluting with acid.

The thus eluted, "connected" antibodies are thus those which had been bound to the IgG F(ab')2 that was prepared from IVIg . These acid elected antibodies represent 0.74% or one in 135 of the IgG antibodies of IVIg originally added to the affinity support. See Table I and page 1702, col.2. Thus, on a per mg IgG basis, what Dietrich et al obtained in their acid eluate was a preparation of antibodies reactive with IgG F(ab')2 that had been enriched by a level of 135.

Regarding reactivity with Tetanus toxoid (TT), Dietrich et al show (Fig 4, left most graph) that the degree of reactivity of the "connected" antibody fraction is about the same as or less than that of the unfractionated IVIg .

From the above considerations, instant claims 1-3 and 8 are anticipated.

Regarding claims 4-5 Dietrich et al show increased reactivity of the elected, "connected" antibodies with myosin, actin, and tubulin (Figure 1). The OD readings therein cannot be readily related to binding activity of the antibodies on a per mg basis;

however, there appears to be, at the least, a marked enrichment of anti-tubulin antibodies (3 across, 2 down in the matrix of graphs). In absence of USPTO testing facilities burden lies on applicant to show a difference. See Ex parte Gray 10 USPQ2d 1922.

Regarding, claims 6-7, Dietrich et al have shown antibody reactivity with myosin, actin and tubulin. They do not determine "connected" antibody binding activity with MBP. Since MBP is a highly conserved protein, one would reasonably expect that the "connected" antibody of Dietrich et al to also bind MBP. See Dietrich et al at page 1703, col.1 regarding reactivity with conserved self-antigens. The burden lies upon applicant to show a difference.

The examiner reasonably considers that applicant be required to show a difference between what is claimed and the "connected" antibody preparation of Dietrich et al. Applicant and Dietrich et al each start with a polyvalent IgG preparation from pooled plasma; applicant uses TEGELINE (Fig 1 and Ex. 1); Dietrich et al use Sandoglobulin (page 1702, col.1); the examiner knows of no substantial difference between these. Applicant couples the whole IgG, while Dietrich et al couple the F(ab')2 fragment of IgG to the solid affinity matrix. The matrix in each case thus includes the V-regions of the antibodies from the IgG preparation. It is the binding of solid-phase coupled V-regions with IVIg liquid phase V-regions that leads to selection of the "connected" antibodies of both applicant (e.g. para spanning pages 3-4) and of Dietrich et al (page 1702, second full para.). Thus the affinity chromatography processes of

both applicant and of Dietrich et al should have selected "connected" antibodies with like inherent properties with respect to their repertoires of cognate antigens.

Claims 1-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Berneman et al (Molecular Immunology 30, 1449, 1993) in light of Kimball.

Berneman et al show a pooled preparation of IVIgG from healthy donors that is subjected to a further purification for IgG on pG-sepharose and then for polyreactive antibodies on DNP-lysine-sepharose. See procedures at page 1500.

Figure 5 shown the reactivities of this preparation before (left most bars) and after (right most bars) adsorbtion on the DNP-lysine-sepharose. The examiner takes reactivity with TNP to represent that also with DNP, since these two haptens cross-react with antibodies to either of these haptens (Kimball).

While the OD values shown in Figure 5 cannot be precisely related to absolute amounts of reactive antibody, it is taken that the results shown are consistent with the enrichment values instantly recited. This assertion is reasonably stated by the examiner, because the adsorbtion on DNP-sepharose executed by Berneman et al is conducted in the same manner exemplified by applicant. It is up to applicant to show a difference. Ex parte Grey 10 USPQ2d 1922.

Regarding the reactivity with TT or HBs antigen, the IVIg donors were healthy, and screening for Hepatitis B was routine for any commercial preparation of IVIg. It is thus inherent that antibodies to HBs were initially at undetectable levels, and the adsorbtion on DNP would not have been expected to enrich for any such antibodies that might have been present. Again, applicant must show a difference.

Applicant must also note that the examiner's assertions regarding enrichment levels recited can be applied with respect to either i) the pG-sepharose purified fraction of Berneman et al or ii) the commercial IVIgG preparation from which the former was prepared. Thus, if a recited level of enrichment does apply with respect to the pG-sepharose prepared fraction, applicant must also show that this level of enrichment does not apply with respect to the commercial IVIgG preparation; note that claim 1 utterly fails to state how many fractionation steps are conducted between starting with "the initial polyvalent Igs" and obtaining the claimed "Ig fraction."

From the above, examiner reasonably considers claims 1-3 anticipated.

Regarding claim 4, note Berneman et al show enrichment of reactivity wich autoantigens actin, myosin and tubulin.

Regarding claims 6-7, Berneman et al show reactivity with MBP(Table 4) but do not show relative degree of enrichment (Fig.5). However, on the basis that they did the same purification step of adsorbtion on DNP sepharose as did applicant, the examiner reasonably asserts that such autoreactivity was present in the adsorbed preparation of Breneman et al. Applicant must show a difference.

Claims 1-3 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Franek et al (Molecular Immunology, 389, 1979).

Franek et al show an affinity purified IgG antibody preparation having binding specificity for DNP. Regarding the degree of purity note page 391, col.2 and Fig.3 teach that, on a per wt basis, the affinity purified preparation has 125x more binding activity.

Regarding reactivity with TT or HBs antigen the reference is silent. However, since the anti-DNP antiserum was isolated from rabbits not intentionally exposed to TT or HBs and since the antiserum was affinity purified on DNP, one would reasonably expect that the affinity purification process would not have enriched for any antibodies against TT or HBs that might have been present.

From the above, instant claims 1-3 are anticipated.

Regarding claim 9, the reference is silent as to reactivity with Ig M or with IgG F(ab')2; however, as argued supra regarding reactivity with TT or HBs, one would not have reasonably expected the affinity purified preparation of Franek et al to have a significant amount of such reactivity.

Claim 25 is allowable over prior art of record. No reference shows a selecting step for an Ig fraction which inhibits MLC activity. No reference provides motivation to conduct such a step.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, PhD whose telephone number is 571-272-0849. The examiner can normally be reached on Monday-Thursday from 8:00a.m to 5:30p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Saunders/tgd

March 29, 2004

David A Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1764